Robust Summaries & Test Plans: 2,4,6-Trimethylphenol; Animal Protection Organizations' Comments

May 27, 2003

Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on the HPV Test Plan for 2, 4, 6-Trimethylphenol

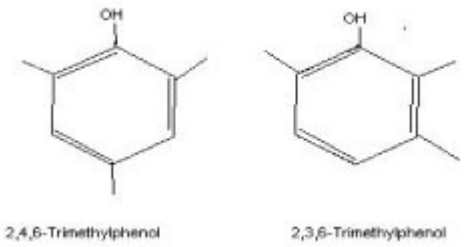
Dear Administrator Whitman:

The following comments on the General Electric Company (GE) High Production Volume (HPV) Chemicals Challenge Program test plan for 2, 4, 6-Trimethylphenol (2, 4, 6-TMP), CAS RN 527-60-6, are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

2, 4, 6-TMP is one of three test plans submitted by Toxicology/Regulatory Services, Inc. on behalf of GE on December 30, 2002. As noted below we object to GE's proposal to conduct OECD Test Guideline 422 (combined Repeat dose/Repro/Developmental screen, which kills at least 675 animals) as the test plan states that no data exists for these endpoints.

By simply scanning the list of HPV Challenge Program Test Plans, GE would have found the test plan for the Alkylphenols category, submitted on May 18, 2001 by Schenectady International, Inc. We recognize that EPA classified this category as too broad, but some of the chemicals in the category can and should be used in the data collection efforts of GE regarding 2, 4, 6-TMP.

Figure 1: Structure Comparison



The most similar chemical in the alkyl phenols group is 2, 3, 6-TMP (CAS RN 2416-94-6). This compound is almost identical to 2, 4, 6-TMP and has similar characteristics, i.e.,

molecular weight, boiling point, melting point, log Kow, water solubility, low acute fish and mammalian toxicity values, and genetic toxicity values all correlate well between these two chemicals. As can be seen from Figure 1 above, both chemicals have a hydroxyl group and three methyl groups attached to one benzene ring. The only structural difference between the two compounds is the position of one of the methyl groups. Past HPV Program test plans, such as the ethylphenols and mixed xylenols categories, both submitted by Merisol USA LLC on July 29, 2002, used analogous structural similarities to justify category inclusion. While data are not available for repeat dose, reproductive or developmental toxicity for 2, 3, 6-TMP, there are a few possible strategies to meet this SIDS data requirement, thus making Test Guideline 422 unnecessary per the Challenge Program and preventing the suffering of at least 675 animals.

There are four chemicals that are similar in structure and have repeat dose/developmental/reproductive data available: p-tert-Butylphenol (CAS RN 98-54-4), p-tert- Octylphenol (140-66-9), 2,6-Di-tert-butylphenol (128-39-2), p-Nonylphenol (84852-15-3) and 2,4,6-Tri-tert-butylphenol (732-26-3). The EPA, in its comments to Schnectady International, Inc., acknowledged the adequacy of these data. Schnectady International, Inc. was, according to their test plan, using category analogy to determine data for the repeat dose, developmental and reproductive endpoints for 2, 3, 6-TMP. Surely 2, 4, 6-TMP could be included in this category as well. Furthermore, if Schnectady International, Inc. has decided to test 2, 3, 6-TMP for these endpoints, GE should collaborate with them and use these data to revise the 2, 4, 6-TMP test plan. At this time, it is unclear whether Schnectady International, Inc. decided to revise their test plan per EPA comments. Data will be generated, either experimentally or by category analogy, for 2, 3, 6-TMP. These data should also then be applied to 2, 4, 6-TMP, and no further testing need be conducted on this chemical.

Collaborating with Schnectady International, Inc. would conserve resources and most importantly, prevent the suffering and death of at least 675 animals. We strongly urge the EPA to reject the plan to use OECD Test Guideline 422 as unnecessary and encourage GE to collaborate with Schnectady International, Inc. The premise applied in our analysis is the key element of the HPV Program's intended use of categories to minimize testing and the killing of animals.

Thus, this test plan from GE is yet another violation of the October 14, 1999 agreement letter, which directs participants to coordinate test plans with one another. This letter states "participants shall maximize the use of scientifically appropriate categories of related chemicals and structure activity relationships," and to "maximize the use of existing and scientifically adequate data to minimize further testing."

Thank you for your attention to these comments. I look forward to a prompt and favorable response to our concerns. I may be reached at 202-686-2210, ext. 335, or via email at kstoick@pcrm.org.

Sincerely,

Kristie Stoick, MPH
Research Analyst

Chad Sandusky, PhD
Director of Research

URL: http://www.epa.gov/chemrtk/246trime/c14218pm.htm